UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,113	04/04/2007	**Kristian Lund Henriksen**	BECK:001	3904

36275 7590 10/13/2010

O'KEEFE, EGAN, PETERMAN & ENDERS LLP
1101 CAPITAL OF TEXAS HIGHWAY SOUTH
#C200
AUSTIN, TX 78746

EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/584,113	HENRIKSEN ET AL.	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *12-18,27-31,and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,19-26,32-48 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is directed to papers filed 07/22/2010.

Claims 1-50 are pending. No claims have been amended, newly canceled or newly amended.

Claims 12-18, 27-31 and 49 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/24/2009.

Claims 1-11, 19-26, 32-48 and 50 have been examined on their merits.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

> invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-11, 19-26, 33-48 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Glagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS).

Claim 1 is drawn to a probiotic tablet comprising at least two zones wherein the first zone comprises a probiotic and a second zone comprises at least one other active

ingredient kept separate from the probiotic in the first zone and wherein the water activity of the probiotic in the first zone is no greater than 0.2 and the water content of the tablet being no less than 0.2% by weight.

Dependent claims include wherein the first zone is free from amounts deleterious to the viability of the probiotic of several ingredients (claims 3-10), wherein the second zone contains iron as an active ingredient (claims 11 and 19), the addition of a desiccant carrier material (claims 20-22), a multi-layer structure (claim 23), first zone free of encapsulated iron , zinc and copper (claims 24-26), specific water contents (claims 33-39), specific water activity (claims 40-44), a water excluding barrier material surrounding the first zone of the tablet (claim 45), including a tablet coating that excludes water (claim 46) and wherein the tablet is stored under specific conditions (claim 47) and wherein the barrier material is a fat or wax based material (claim 48).

Glagau et al teach a two-part micronutrient product, useful as a dietary supplement and for treatment of disease which comprises a probiotic component and secondary ingredients in another component (abstract). The product may be formulated as multi-component single tablet (page 5, 4th paragraph) and includes wherein the first and second components are kept separate from each other (page 2, 5th paragraph). The second portion is taught to potentially contain many different secondary ingredients and includes combinations of iron and vitamins B6 and C (page 8). Adjuvants to be added to the probiotic include starch (page 8 example 1) and other ingredients that improve the bioavailability and shelf life of the probiotic (page 6, 1st paragraph). The first

component is kept free of amounts of any substances that are deleterious to the viability of the probiotic.

Glagau et al do not appear to explicitly describe a zoned single tablet.

Bakulesh et al teach a method of making a pharmaceutical tablet formulation of a probiotic that is kept separate from secondary active ingredients by the addition of barrier materials (page 13). This is interpreted as a multi-zoned tablet. Exemplary barrier materials are taught to include oil/wax based materials (page 15, number 9).

It would have been obvious to make a multi-zoned single tablet for the product of Glagau et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because Bakulesh et al teach that it is known in the art to formulate a probiotic tablet with barrier materials to keep the primary ingredient of the probiotic separate from the potentially deleterious secondary ingredients. One of ordinary skill in the art would have been motivated by the teachings of Giagau et al as well since this reference includes a formulation of the multi-component product that includes the form of one tablet (page 5 4th paragraph) as well as the need to keep the probiotic separate from the nutrients in the second component (page 2 paragraph 5).

Glagau et al are silent with regard to the water content and water activity of the probiotic composition.

Runge et al teach dried microorganism cultures that are compressed and used for foodstuffs and feedstuffs (abstract). Preferred probiotics include Lactobacillus species as well as other genera (column 6 lines 19-44 of US 7,037,708). Dry preparations having low moisture content (of from about 2 to 3% by weight of water)

corresponding to a water activity of from 0.03 to 0.15 are provided by spray drying and have survival rates of up to 60% after storage for 1 year at ambient temperatures and ambient air conditions (column 5 lines10-21). Tablet formulations of the dried microorganisms are taught as suitable and include the addition of tabletting aids such as PVP (column 11 lines 47-67) and desiccants (column 10 lines 8-18). Coating materials are added to hinder the ingress of moisture to the dry preparation (column 12 lines 24-26). Storage in suitable containers is taught as well (column 18 lines 1-10).

It would have been obvious to apply the formulation methods of Runge et al to the tableted probiotic composition of Glagau et al with regard to the water content, water activity and suitable additives of the different zones. One of ordinary skill in the art would have been motivated to do so because Runge et al teach that these parameters are beneficial to the viability and shelf life of a dried probiotic composition. Modifying the water activity to 0.02 would have been a matter of routine optimization and experimentation as the artisan of ordinary skill would be motivated to attain a dry microorganism with the greatest stability and viability. The use of a storage container with a desiccant would have also been obvious as Runge et al teach the benefit of adding desiccant materials and storing the product in suitable storage containers as well. One of ordinary skill in the art would have had a reasonable expectation of success because both Glagau et al and Runge et al are producing tableted probiotic compositions for oral administration.

Therefore the combined teachings of Glagau et al, Bakulesh et al and Runge et al render obvious Applicant's invention as claimed.

Claim 2 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Glagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Belicova et al (Folia Microbiol. 2004).

Claim 2 includes wherein the first zone also contains selenium as an additional active agent.

The combined teachings of Glagau et al, Runge et al and Bakulesh et al render obvious the claimed invention as described above, but do not specifically include wherein selenium is included in the first zone with the probiotic component.

Belicova et al teach that the antimutagenic activity of probiotic bacterium *Enteroccus faecium* was enhanced by the addition of selenium. Selenium enriched probiotic bacterium *E. faecium* can be considered as a food supplement with beneficial health benefits (page 304, last paragraph).

Therefore it would have been obvious to include selenium in the first zone with the probiotic component of the Glagau et al composition because Belicova et al teach that selenium enhances the antimutagenic activity of probiotic bacterium *Enteroccus faecium* and selenium enriched probiotic bacterium *E. faecium* can be considered as a food supplement with beneficial health benefits (page 304, last paragraph). One of

ordinary skill in the art would have had a reasonable expectation of success because Glagau et al were also using the probiotic bacterium *Enteroccus faecium* as well (page 2, last paragraph).

Therefore the combined teachings of Glagau et al, Runge et al, Bakulesh et al and Belicova et al render obvious Applicant's invention as claimed.

Claims 32 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Glagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Andoh et al (EP 0255725).

Claim 32 includes wherein the tablet has a multitude of granules constituting the first zone surrounded by a matrix, and wherein the matrix constitutes a second zone **or** wherein the matrix also contains a multitude of granules constituting the second zone.

The combined teachings of Glagau et al, Runge et al and Bakulaesh et al render obvious the claimed invention as described above, but do not specifically include a formulation that includes zones of matrix and compressed granules. However, Giagau et al do indicate that additives that offer an improvement or benefit to the final product formulation may be included (page 6).

Andoh et al teach a sustained release multi-granule tablet useful in the field of therapy. The invention is concerned with a tablet of the multiple unit type (different zones) in which sustained release granules are contained as a unit (page 2, 1st paragraph). Water resistant coatings (barriers) are applied in layers between the different zones (page 3).

Therefore one of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the formulation strategies of Andoh et al to the probiotic tablets of Glagau et al because Andoh et al teach that these are suitable for the formulation of multi-component tablets for pharmaceutical use.

Therefore the combined teachings of Glagau et al, Runge et al, Bakulesh et al and Andoh et al render obvious Applicant's invention as claimed.

Claim 50 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Glagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Cavaliere et al (EP 0956858- from IDS).

Claim 50 includes wherein the first zone disintegrates at a faster rate than the second zone and is no more than 50% of the total disintegration time.

The combined teachings of Glagau et al, Runge et al and Bakulesh et al render obvious the claimed invention as described above, but do not specifically include

different disintegration times of the different zones. Glagau et al do indicate that additives that offer an improvement or benefit to the final product formulation may be included (page 6) and Runge et al indicate that formulating the product to allow for a more rapid release of the microorganism is suitable as well (column 11 lines 7-45).

Cavaliere et al disclose a two-layer tablet comprising a quick release layer and a slow release layer, both containing a dried probiotic culture. The quick release layer disintegrates in a lapse of time of 10-25 minutes whereas the slow release layer disintegrates in a lapse of time of 25-50 minutes (page 4 paragraphs 28-29).

Therefore one of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the formulation strategies of Cavaliere et al to the probiotic tablets of Glagau et al because Cavaliere et al teach that these are suitable for the formulation of multi-component probiotic tablets for pharmaceutical use.

Modifying the release characteristics of the tablet in order to optimize the therapeutic result would have been a matter of routine optimization and experimentation, the artisan of ordinary skill motivated to release the probiotics in a manner that increases the effectiveness of the probiotic microorganisms.

Therefore the combined teachings of Glagau et al, Runge et al, Bakulesh et al and Cavaliere et al render obvious Applicant's invention as claimed.

Response to Arguments

Applicant's arguments filed 07/22/2010 have been fully considered but they are not persuasive.

Applicant argues that Glagau et al (previously misspelled as Giagau et al) does not teach a probiotic formulation that includes a single tablet formulation. Applicant asserts that Glagau et al requires a product formulation wherein the probiotic part is kept completely separate in a different formulation than the additional nutritive components. Applicant asserts that because Glagau et al teaches a range of 0 to 10 tablets that Gaglau et al could not have intended their product to be present in a single tablet.

This is not found persuasive because Glagau et al clearly provides for a product that can be from 0 to 10 tablets which would allow for the product to be in a formulation other than a tablet (such as a liquid or granule) or as a single tablet. Glagau et al do teach that the probiotic needs to be kept separate from the nutritive components and the teaching of a multi-zoned tablet, as disclosed by Bakulesh et al, is a known option in the art of tableted probiotics thus making it a known viable option.

Applicant argues that the Examiner has not pointed out any disclosure of the presence of nutritionally active ingredients in a second zone.

This is not found persuasive because the Examiner has pointed out that the separating of components by the forming of a multi-zoned tablet is a known and viable modification in the art of tableted probiotic compositions as described by the cited prior art.

Applicant argues that the assertions regarding stability in Bakulesh et al are unsupported by any tests or data and seem to lack credibility. Applicant asserts that evidence that the reference is unreliable is provided on page 22 wherein the example asserts that a liquid formulation comprising antibiotics and microorganisms would be stable for up to 7 days.

This is not found persuasive because the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference; nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

The example on page 22 of the Bakulesh et al reference may or may not be enabled, but the disclosure in Bakulesh et al of a multi-zoned tablet that provides for a formulation wherein probiotics are kept separate from other desired components is clearly enabled and suitable as a teaching to suggest to one of ordinary skill in the art that a single tablet formulation is possible for the Glagau et al method and composition.

Applicant argues that the essential point is that nothing is taught in either Glagau et al or Bakulesh et al as to the water content and water activity characterizing the present invention. Applicant asserts that the Runge et al teaching with regard to water content and water activity of a probiotic tablet can not be applied to either Glagau et al or Bakulesh et al because Runge et al does not include the addition of nutriotionally active ingredients.

This is not found persuasive because that fact that Glagau et al and Bakulesh et al are silent with regard to water content or water activity would suggest that one of ordinary skill in the art would look to teachings in the art of dried probiotics, such as Runge et al, for the suitable parameters to be applied.

Applicant is directed to pages 12-13 of *KSR v Teleflex* (500 US ___ 2007) " … the Court has held that a "patent for a combination which only unites old elements with no change in their respective functions . . . obviously withdraws what is already known into the field of its monopoly and diminishes the resources available to skillful men." Great Atlantic & Pacific Tea Co. v. Supermarket Equipment Corp., 340 U. S. 147, 152 (1950). This is a principal reason for declining to allow patents for what is obvious. The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." "When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either ***in the same field or a different one(emphasis added)***. If a person of ordinary skill can implement a predictable variation, §103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill." Clearly in the instant case the use of a formulations and water parameters disclosed in the prior art as suitable for a tableted probiotic composition would have been obvious at the time the invention was made.

Applicant asserts that a skilled reader familiar with the practice of drying probiotics would read Glagau et al and Bakulesh et al and would suppose that extreme drying would be needed in a formulation based on such a combination of teachings. Applicant asserts that one skilled in this art would not be motivated to apply the teachings of Runge et al because Runge et al does not teach applying their parameters to two part tablet formulations.

This is not found persuasive because the teaching of Runge et al is applicable to any formulation that contains a probiotic and wishes to maintain the viability of that probiotic in the formulation.

Applicant asserts that the skilled reader could not have a reasonable expectation of success in maintaining the ability of the probiotic microorganisms to withstand long term storage based on the teachings of Runge et al. Applicant asserts that the reasonable expectation would have been that the relatively high water content of such a product would facilitate the action of the other nutritionally active ingredients in adversely affecting the microorganisms and nothing in either of the two references Glagau et al and Bakulesh et al would suggest otherwise.

This is not found persuasive because this argument is merely the argument of counsel and is unsupported by evidence or declarations of those skilled in the art. Counsel's arguments cannot take the place of objective evidence. *In re Schulze*, 145 USPQ 716 (CCPA 1965); *In re Cole*, 140 USPQ 230 (CCPA 1964): and especially *In re Langer*, 183 USPQ 288 (CCPA 1974). There is nothing in the teachings of cited prior art references that suggests that keeping the probiotic formulations at a water content and

activity favorable to the probiotic viability would have caused the additional ingredients (kept separate in a multi-zone tablet as suggested by Bakulesh et al) to become endowed with properties that would render the composition unstable as asserted by Applicant.

Applicant argues that there is no logical basis for the skilled person to assume that conditions taught to be suitable in the absence of deleterious ingredients will also work in the presence of such ingredients.

This is not found persuasive because dried probiotics perform best under optimal moisture conditions and this is clearly taught in the prior art. Whether these conditions are in the presence of deleterious ingredients or not does not change the fact that probiotics perform best when their moisture content is optimal. In addition, the teachings of the prior art suggest that probiotics be administered in a formulation that is optimal to the viability and stability of those probiotics and suggest that keeping the probiotics separate from desired but deleterious components is best and that a multi-zone tablet is one option available. It is not illogical to combine the teachings in the prior art of tableted probiotic therapeutic compositions in order to optimize the therapeutic properties of that composition. The combining of features taught to be beneficial in the art of probiotics is a logical and obvious basis for any modification.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg